factors. RR of CV events is shown in the table.
Conclusion: Current ERT use among older women was associated with fewer myocardial infarctions and "HERS endpoints", but there was no association with all cause mortality or stroke. Past ERT use was associated with lower all cause mortality, but there was no association with CV events. The observed associations may reflect a healthy-user effect. Clinical trials will be necessary to assess the effect of ERT in older women.

Fully Adjusted Cox Model of CV Events (RR(95%CI))

	Past ERT	Current ERT
Death	.72 (.57,.90)	1.03 (.76,1.40)
Myocardial Infarction	.90 (.66,1.23)	.44 (.23,.84)
Stroke	.84 (.62,1.13)	.94 (.60,1.45)
"HERS Endpoint" (nonfatal MI or CHD death)	.82 (.64,1.06)	.54 (.34,.86)

1113-150 **Chronic Vitamin C Supplementation Improves Endothelial Function in Diabetic Patients With Coronary Artery Disease**

Charalambos Antoniades, Dimitris Tousoulis, Costas Tentolouris, Kyriakoula Marinou, Athanasios Trikas, Stella Brilli, Christos Pitsavos, Christodoulos Stefanadis, Pavlos Toutouzas, *Cardiology Unit, Hippokration Hospital, Athens University Medical School, Athens, Greece.*

Background: Coronary artery disease (CAD) as well as diabetes mellitus (DM), are both known to be associated with endothelial dysfunction. Oxidative stress is considered to be one of the most important mechanisms involved in the pathogenesis of endothelial dysfunction in CAD and DM. In this study we investigated whether treatment with the antioxidant vitamin C improves endothelial function in patients with type I or II DM and CAD.
Methods: In a double-blind placebo-controlled study, 48 patients (42 males, 6 females, aged 66±1.3 years) with CAD and DM, were enrolled. 22 of them were of type I DM and 26 of type II. 18 diabetic patients (7 with type I DM (group A) and 11 with type II DM (group B)) were treated with vitamin C 2g/day for 4 weeks. The remaining (15 with type I DM (group C) and 15 with type II DM (group D)) received placebo for 4 weeks. Forearm blood flow was measured using venous occlusion strain-gauge plethysmography, at baseline and after treatment. Endothelium dependent flow mediated vasodilation (FMD) was expressed as the % change from baseline to post reactive hyperemia blood flow. Endothelium independent flow (NTG%) was expressed as the % change from baseline to post sublingual nitroglycerin administration flow.
Results: Basal blood pressure, heart rate, body weight, basal forearm blood flow and NTG% remained unchanged in all groups. All values are expressed as mean±SEM. FMD was similar between patients with type I (53.9±3.3%) and type II (57.8±6.0%, p=NS) DM. After treatment, RH% was significantly increased in groups A (from 54.2±7.3 to 73.1±7.1% p<0.05) and B (from 66.5±11.7 to 84.3±15.1% p<0.05) while remained unchanged in groups C (from 53.1±4.2 to 50.1±8.2% p=NS) and D (from 55.8±11.6 to 58.3±10.1% p=NS).
Conclusions: Chronic administration of vitamin C seems to improve endothelial function in patients with combined coronary artery disease and diabetes mellitus of type I or II. These findings indicate a possible beneficial role of antioxidant vitamin C in diabetic patients with coronary artery disease.

FEATURED ORAL PRESENTATION

830FO Featured Oral Session...Stress Testing and Prognosis: Non-ST Segment Parameters

Monday, March 18, 2002, 2:00 p.m.-3:30 p.m.
Georgia World Congress Center, Room 367W

2:15 p.m.

830FO-2 **The Yield of Screening Stress Myocardial Perfusion Imaging in Asymptomatic Diabetics**

Todd D. Miller, Navin Rajagopalan, David O. Hodge, Robert L. Frye, Raymond J. Gibbons, *Mayo Clinic, Rochester, Minnesota.*

Background: Diabetics have a higher prevalence of silent coronary artery disease (CAD) than nondiabetics and a prognosis similar to that of patients with established CAD. Nonetheless, screening stress testing in asymptomatic persons without known CAD including diabetics is not well established according to the ACC/AHA Guidelines for Exercise Testing.
Methods: The results of exercise and pharmacologic single photon emission computed tomography (SPECT) imaging were analyzed in 27,179 patients without known CAD who underwent testing between January 1986 and December 2000. Patients were grouped by symptom and diabetes status. SPECT scans were categorized as abnormal or not and "high-risk" (on the basis of previously published criteria) or not.
Results:

Subset	Number	Age (yrs ± SD)	Male (%)	Abnormal SPECT (%)	High-risk SPECT (%)
Symptomatic, nondiabetic	16,196	62±15*	53*	44*	13*
Symptomatic, diabetic	2994	63±11*	53*	59	22
Asymptomatic, nondiabetic	6248	63±11*	73*	46*	11*
Asymptomatic, diabetic	1741	60±13	70	59	20

*p ≤ 0.004 vs asymptomatic diabetic

Insulin use did not further stratify asymptomatic diabetics for abnormal SPECT (57% insulin vs 60% no insulin, p=0.15) or high-risk SPECT images (20% insulin vs 19% no insulin, p=0.59). In asymptomatic diabetics who underwent exercise stress (52%), a positive ECG occurred in 29%.
Conclusions: In asymptomatic patients referred for screening stress SPECT imaging, diabetics are slightly younger and more frequently female than nondiabetics but have a significantly higher prevalence of abnormal and high-risk SPECT scans. Both abnormal and high-risk scans are more common in asymptomatic diabetics than even in symptomatic nondiabetics.

2:30 p.m.

830FO-3 **Comparison of Noninvasive Cardiac Testing in 903 Asymptomatic Men: Correlation With Coronary Angiography and With Clinical Events at Two and Five Years**

Patrick J. Fitzsimmons, Ants Palm-Leis, William T. Thompson, William B. Kruyer, *USAF School of Aerospace Medicine, Brooks AFB, Texas.*

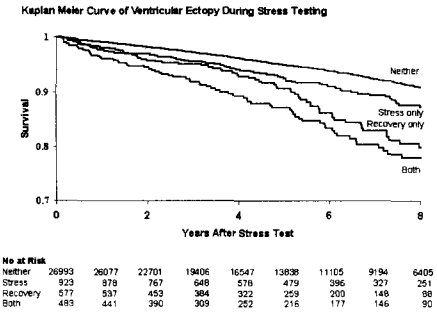
Background: Noninvasive techniques may be used to screen asymptomatic subjects for coronary artery disease (CAD). However, the accuracy of these tests is significantly influenced by the low prevalence of CAD in asymptomatic populations. We sought to define the accuracy of three noninvasive tests for predicting significant CAD and cardiac events in a population of asymptomatic men.
Methods: From a database of 1487 asymptomatic military aviators who had coronary angiography performed for occupational indications and had clinical follow-up, we identified 903 who had all three noninvasive tests prior to angiography - treadmill, stress thallium imaging and coronary artery fluoroscopy for detection of coronary calcification. Sensitivity, specificity and positive and negative predictive values were calculated for each test for the presence of significant CAD (maximum lesion >50% stenosis). Cardiac event rates at two and five years were determined for abnormal versus normal test. Cardiac events considered were cardiac death, nonfatal myocardial infarction and coronary revascularization.
Results: Mean age at coronary angiography was 43.7 (+/-6.2) years and mean follow-up was 11.8 (+/-3.8) years. Sensitivity, specificity and positive and negative predictive values for the presence of significant CAD were: treadmill 54%, 49%, 16% and 86%; thallium 55%, 62%, 21% and 89%; and fluoroscopy 68%, 71%, 29% and 93%. Average annual cardiac event rates at two and five years for abnormal test were: abnormal treadmill 1.0%/yr and 0.5%/yr, abnormal thallium 1.0%/yr and 0.6%/yr, and positive coronary artery fluoroscopy 1.6%/yr and 1.3%/yr. For normal test, event rates at two and five years were: normal treadmill 0.3%/yr and 0.5%/yr, normal thallium 0.5%/yr and 0.5%/yr, and negative fluoroscopy 0.2%/yr and 0.1%/yr.
Conclusion: As expected, all three noninvasive tests were independently poor predictors of significant CAD and cardiac events in this low CAD prevalence population. For all parameters examined, detection of coronary calcification by routine fluoroscopy performed better than treadmill and thallium, both for prediction of anatomic disease and for cardiac events at two and five years of follow-up.

2:45 p.m.

830FO-4 **Ventricular Ectopic Activity Predicts Mortality When It Occurs During Recovery, but Not Just During Exercise**

Joseph Frolkis, Claire E. Pothier Snader, Eugene H. Blackstone, Michael S. Lauer, *Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: Ventricular ectopy (VEA) induced by exercise predicts death in population-based cohorts. We examined the prognostic importance of VEA during exercise and recovery, when reactivation of parasympathetic activity occurs. We hypothesized that VEA during recovery would predict death better than VEA during exercise.
Methods: We followed for 5.3 years 28,976 patients (age 56±11, 70% male) who underwent treadmill exercise testing and were without heart failure, valve disease, atrial fibrillation, VEA history, or pacemakers. VEA was defined as: > 7 VPCs/minute, ventricular bigeminy or trigeminy, ventricular tachycardia, or ventricular fibrillation.
Results: VEA during exercise only occurred in 923 patients (3%), during recovery only in 577 (2%), and during exercise and recovery in 483 (2%). There were 1801 deaths (6%). In univariate analyses, VEA during exercise predicted death (11% vs. 6%, hazard ratio [HR] 1.9, 95% CI 1.6-2.2, P<0.0001), but VEA during recovery was a stronger predictor (13% vs. 6%, HR 2.4, 95% CI 2.1-2.9, P<0.0001) (Figure).



After accounting for age, gender, risk factors, medications, coronary history, exercise capacity, chronotropic response, and heart rate recovery, VEA during recovery remained predictive of death (adjusted HR 1.5, 95% CI 1.2-1.8, P<0.0001), but VEA during exercise was not predictive (adjusted HR 1.1, 95% CI 0.9-1.4, P=0.18).**Conclusion:** As we hypothesized, VEA during recovery after exercise predicts mortality, but VEA only during exercise does not.

3:00 p.m.

830FO-5 Exercise-Induced Ventricular Premature Beats Are Associated With Increased Cardiovascular Mortality: The Framingham Heart Study

Ali Morshedi-Meibodi, Jane Evans, Daniel Levy, Martin G. Larson, Ramachandran Vasan, *NHLBI's Framingham Heart Study, Framingham, Massachusetts, Boston University School of Medicine, Boston, Massachusetts.*

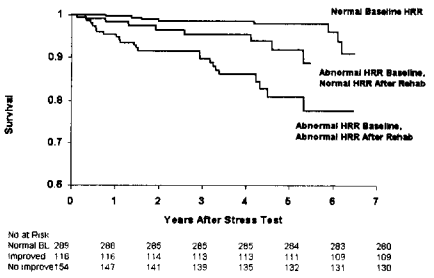
Background: There is controversy regarding the prognostic impact of exercise-induced ventricular premature beats (VPB). While earlier studies reported no adverse relation, the Paris Prospective Study recently reported an increase risk of death in men with exercise-induced VPBs.
Methods: We evaluated 2,840 Framingham Offspring Study subjects (1,388 men, mean age 43 years) who were free of cardiovascular disease and underwent a heart rate-limited exercise test according to the Bruce protocol during a routine examination. 780 subjects (27%) had VPBs during the exercise (median of 0.22 VPBs/minute of exercise). Subjects were divided into three groups based on the numbers of VPBs/minute of exercise: those without any VPBs, those below (low frequency VPBs) and those above the median (high frequency VPBs). Cox proportional hazard regression models incorporating established risk factors (age, sex, diabetes, hypertension, smoking, total and HDL cholesterol) and adjusting for interim cardiovascular disease (CVD) events were used to examine the association of exercise-induced VPBs at the baseline examination with risk of death due to coronary heart disease (CHD), CVD (including CHD and other vascular events), and all-cause mortality on follow up.
Results: On follow up (mean 15 years), 159 subjects died (38 CVD deaths [31 men], 29 CHD deaths [24 men]). Exercise-induced VPBs were associated with increased risk of all-cause mortality [multivariable HR for trend across 3 groups of 1.38, 95% CI, 1.14-1.65], CHD-death [HR 1.82, 95% CI, 1.20-2.74] and CVD-death [HR 1.91, 95% CI, 1.33-2.73]. The high VPB frequency group was associated with the greatest risk of all three outcomes.
Conclusions: In our large community-based sample of men and women, exercise-induced VPBs identified a group at increased risk of death secondary to CHD, CVD, and all-cause mortality. Additional studies are needed to examine the utility of the exercise-induced VPBs for risk stratification.

3:15 p.m.

830FO-6 Heart Rate Recovery Improved in a Cohort of Adults After Cardiac Rehabilitation

Ema Obenza Nishime, Christopher R. Cole, Gregory S. Wallace, Robert J. Rosnick, Claire E. Pothier Snader, Eugene H. Blackstone, Gordon Blackburn, Michael S. Lauer, *Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: An abnormal heart rate recovery after exercise predicts mortality. As exercise modulates autonomic function and heart rate recovery reflects vagal tone, we hypothesized that cardiac rehabilitation would favorably impact heart rate recovery.
Methods: Consecutive adults (n=595, 61±11 years, 78% male) who underwent symptom-limited exercise tests before and after Phase II cardiac rehabilitation were studied. Heart rate recovery (HRR) was the difference of heart rate at peak exercise and one-minute later with ≤ 12 bpm abnormal.
Results: HRR improved from a median of 13 bpm before rehabilitation to 17 bpm afterwards (P<0.0001). There were 287 adults (48%) with abnormal baseline HRR; 161 (56%) were still abnormal afterwards. Predictors of failure to improve HRR included older age (for 10 years, adjusted Odd Ratio [OR] 1.3, 95% CI 1.0-1.7, p=0.03), lesser change in exercise capacity (for 1.5 METs, adjusted OR 1.3, 95% CI 1.1-1.6, p=0.002). During 4 years, there were 42 deaths. After adjusting for age, gender, and change in exercise capacity, abnormal baseline HRR predicted death (12% vs. 3%, adjusted HR 4.0, 95% CI 1.8-8.8, p=0.0006). Failure to improve an abnormal HRR tended to predict higher mortality (adjusted HR 2.0, 95% CI 0.9-4.3, P=0.08) (Figure).



Conclusion: Heart rate recovery improved in patients after cardiac rehabilitation. Although we cannot exclude regression to the mean, the tendency of an improved HRR to predict lower mortality suggests that this was prognostically meaningful.

POSTER SESSION

1133 Myocardial Function/Adrenergic Receptors

Monday, March 18, 2002, 3:00 p.m.-5:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1133-137 Myocardial Overexpression of the Cardiac b-Adrenergic Receptor Kinase-1 Inhibitor (BARKI) Delay the Development of Cardiomyopathy Induced by Myocardial Expression of Monocyte Chemo-Tactic Protein-1 (MCP-1)

Samer J. Khouri, Philip Binkley, Walter Koch, Pappachan Kolattukudy, *Ohio State University, Columbus, Ohio, Duke University, Durham, North Carolina.*

Background: Targeted expression of MCP-1 in the cardiomyocytes induces cardiomyopathy in a murine model. We hypothesized that overexpression of BARKI in these MCP-1 mice may delay the progression of ventricular remodeling. **Methods:** Studies were performed on mice with targeted myocardial expression of BARKI, MCP-1, BARKI and MCP-1 (MCP-BARKI) and wild-type mice as controls. 2D and M-mode echo were performed at baseline, 1 and 2 month. **Results:** At baseline MCP-1 and MCP-BARKI mice did not have a significant difference in mass 68.4 ± 0.6 & 68.6 ± 0.7 mg nor in EF 42 ± 5 & 44 ± 3 % and they were significantly different from BARKI mice and controls (Figures). The MCP-BARKI and MCP-1 mice increased LV mass to the same extent at one month. However, at two months, the LV mass was significantly greater in the MCP-1 mice as compared to MCP-BARKI mice 92.9 ± 8.3 and 80.0 ± 1.3 mg, respectively. BARKI and control mice had mild increase in cardiac mass, but significantly different from MCP-1 and MCP-BARKI mice 69.9 ± 0.4 and 70.9 ± 1.7, respectively. The EF did not show significant change over time (figure 2). **Conclusion:** βARKI overexpression does not preserve myocardial contractility in mice with cardiomyopathy that express MCP-1, but has a significance effect on the cardiac mass. This suggests a significant influence of BARKI overexpression in preventing cardiac remodeling. This may suggest a novel molecular target for future therapies targeted at the prevention of progressive ventricular remodeling in patients with heart failure.

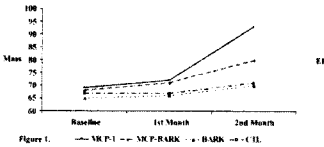


Figure 1.

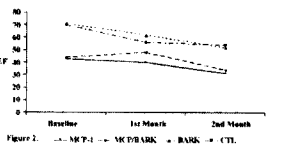


Figure 2.

1133-138 Down-Regulation of Sodium Current in Heart Failure: Rescue by Beta-Blockers

Albertas I. Undrovinas, Victor A. Maltsev, Hani N. Sabbah, *Henry Ford Heart and Vascular Institute, Detroit, Michigan.*

Background: Ion channel remodeling is believed to provide a substrate for ventricular arrhythmias in heart failure (HF). We recently showed that Na^+ channels (NaCh) responsible for excitation generation and propagation in the heart are down-regulated in chronic infarction-induced dog HF model, a feature that suggests possible involvement of these channels in ventricular arrhythmias. While β-blockers (BB) are known to significantly reduce the risk of the ventricular arrhythmias and sudden cardiac death in patients with HF, the cellular and ionic mechanisms of this beneficial effect remain unknown. In this study, we tested the hypothesis that BB prevent NaCh downregulation in chronic HF.
Methods: Studies were performed in cardiomyocytes isolated from dogs with chronic HF produced by multiple sequential intracoronary microembolizations. In addition to marked LV systolic and diastolic dysfunction, dogs with chronic HF also manifests spontaneous ventricular arrhythmias and sudden cardiac death occurs in ~13% of HF animals. To study the effects of BB on the regulation NaCh, HF (LV ejection fraction 28±1%) was produced in 12 dogs. Six HF dogs were treated for 3 months with carvedilol (1 mg/kg, twice daily) and 6 were untreated and served as controls. In addition, cardiomyocytes from 9 normal dogs were used for comparison. At the end of 3 months of therapy, mid-myocardial cardiomyocytes were isolated from the LV free wall. The whole-cell maximum Na^+ current (I_{Na}) was measured using patch-clamp technique in symmetrical Na^+ solutions ($[Na]_i=[Na]_o=5mmol/L$) at room temperature. Chronic treatment with carvedilol restored I_{Na} density in dogs with HF. I_{Na} density in carvedilol dogs was significantly higher compared to that of untreated HF dogs (46.4±0.9 pA/pF vs. 33±3.3 pA/pF, P=0.008) and was similar to that of normal dogs (48.5±5.1 pA/pF). The voltage dependence of steady-state inactivation and activation of I_{Na} remained unchanged in both carvedilol-treated and untreated HF dogs.
Conclusion: Down-regulation of NaCh in ventricular cardiomyocytes caused by chronic HF in dog can be prevented by a chronic therapy with β-blockers.